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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/082,815	02/22/2002	Michael Sworin	2791.1003-007	1636

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EXAMINER	
LY, CHEYNE D	
ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 09/30/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/082,815	SWORIN ET AL.	
	Examiner	Art Unit	
	Cheyne D Ly	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *July 31, 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *53-115* is/are pending in the application.

4a) Of the above claim(s) *84-115* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *53-83* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *53-115* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicant's election of Group I, claims 57-83, Species: A, *in vivo*; B, peptide; C, computationally, filed July 31, 2003, is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. The requirement is still deemed proper and is therefore made FINAL.

3. Claims 57-83, Species: A, *in vivo*; B, peptide; C, computationally, are examined on the merits.

Information Disclosure Statement

4. The information disclosure statements, filed September 25, 2002 and October 01, 2002, fail to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each U.S. and foreign patent; each publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It is noted that this instant application file lacks the documents listed on the said information disclosure statements. The information disclosure statements have been placed in the application file, but the information referred to therein have not been considered.

OBJECTIONS

5. The title of the invention is not descriptive because the instant title is directed to inhibitors while the claimed subject matter is directed to a method. A new title is required that is clearly indicative of the invention to which the claims are directed.

CLAIM REJECTIONS - 35 U.S.C. § 112, SECOND PARAGRAPH

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

7. Claims 59, 60, 73, and 74 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

8. Specific to claims 59, line 9; 60, line 3; 73, line 9; and 74, line 3, the phrase "improved inhibition" causes the claims to be vague and indefinite because it is unclear as to what is being used to consider the inhibition of a molecular interaction has been improved (reduction in interaction between ligand and target protein, or change in target protein conformation). Clarification of the metes and bounds of the instant claims is required.

LACK OF ENABLEMENT UNDER 35 U.S.C. § 112, FIRST PARAGRAPH

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 57-83 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a interleukin-2 receptor (page 9, lines 24-29) and MCP1 (page 12, line 22 to page 15, line 11), does not reasonably provide enablement for any macromolecular ligand and target protein complex. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

11. Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986) and

reiterated by the Court of Appeals in In re Wands, 8 USPQ2d 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. The Board also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for a prima facie case is discussed below.

12. Applicant discloses the targeting group is based on a molecule designed from a model of the target protein/macromolecular ligand complex. Methods of preparing such models are well known in the art and include computational models such as x-ray crystal structures (page 11, lines 2-7). It is acknowledged that the applicant has disclosed information to enable one skilled in the art to practice the claimed method as directed to interleukin-2 receptor (page 9, lines 24-29) and MCP1 (page 12, line 22 to page 15, line 11) based on data derived from x-ray crystal structure modeling. However, a method that relies on data from an unpredictable art such as protein crystallization would require clear and precise guidance for one skilled in the art to reliably use the said method. It is well documented that protein crystallization is in essence a trial-and-error method, and the results are usually unpredictable (Drenth, J.). Further, as recently as November 1, 2002, Science published a New Focus article depicting the current state of the art for protein crystallization that supports the unpredictability of the art. In essence, protein crystallization is still a trial and error process because the current technology for producing protein for the crystallization process is unpredictable, which results in high failure rate for

proteins that are being crystallized. Therefore, researchers continue to have trouble generating sufficient protein required for the crystallization process (New Focus, Science, 2002). Accordingly, it would be unpredictable for one skilled in the art to practice the claims method with any other macromolecular ligand and target protein complex beyond the ones of the instant case wherein data is derived from crystal structure modeling. In light of the difficulty of the protein crystallization process, it is, therefore, unreasonable to expect one skilled in the art to use the information disclosed for interleukin-2 receptor (page 9, lines 24-29) and MCP1 (page 12, line 22 to page 15, line 11) to practice the claimed method with other proteins without undue experimentation.

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 57-63, 65-67, 70-77, 79-81, and 83 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Ladner et al. (US 5,223,409 A).

3. Ladner et al. discloses a method for identifying a compound (inhibitor) (Abstract etc.) comprising "epitode libraries" (analogs) (column 5, lines 63-68 and column 41, lines 20 to column 43, line 10) wherein the protein's constituent segments are held to more or less that conformation (stabilized) unless it is perturbed by denaturant (inert linking group) and if a unconstrained peptide has biological activity, the peptide ligand will be in a random coil until it comes into proximity with its receptor (column 26, lines 1-12). The novel proteins may be

coupled directly or indirectly, covalently, or non-covalently, to a label, carrier, or support (column 105, lines 51-54) in *in vivo* analysis (column 112, lines 23-66). The dissociation constant is preferably greater than 0.10 *uM* and P is the binding protein and A or B represent bind ligands (column 15, lines 13-22; and column 16, lines 22-26), as in instant claims 57 and 71, steps a) and b); and claims 58, 70, 72, and 83.

4. The method of Ladner et al. comprises the preparation of variegated population of proteins (analogs); causing the protein to be displayed on the surface; contacting analogs with target material so that potential binding domains and target material may interact; separating from those that do not bind; the population may be used to select for binding to a first target and subsequent targets (column 10, lines 14-68), and the candidate protein must meet specified conditions (column 20, lines 30-54), as in instant claim 1, steps c)-d); claim 71, steps c)-d); claims 59-61, 73-75, and 81.

5. The target molecule is selected from 3D structures derived from computer or theoretical modeling (column 11, lines 59-65), as in instant claims 62, 63, 76, and 77.

6. The method of Ladner et al. is directed to particles that are metabolically inert (column 54, lines 35-36) and cleavable (column 3, lines 25-30); and degradable (column 98, lines 38-40), as in instant claims 65-67, and 79.

7. The binding protein of Ladner et al. has a molecular weight of approximately 23,000 daltons (amu) (column 15, lines 37-39), as in instant claim 80.

CONCLUSION

8. NO CLAIM IS ALLOWED.

9. Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located

in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 193), and 1157 OG 94 (December 28, 1993) (see 37 CFR § 1.6(d)). The CM1 Fax Center number is either (703) 308-4242 or (703) 305-3014.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to C. Dune Ly, whose telephone number is (703) 308-3880. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

11. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, Ph.D., can be reached on (703) 308-4028.

12. Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instruments Examiner, Tina Plunkett, whose telephone number is (703) 305-3524 or to the Technical Center receptionist whose telephone number is (703) 308-0196.

C. Dune Ly
9/22/03

ARDIN H. MARSCHEL
PRIMARY EXAMINER